

# FIG. 1

DNA sequence for human  
preproparathyroid hormone.

10 30 50  
ATGATHCCNGCNAARGAYATGGCNAARGTNATGATHGNTATGYTNGCNATHTGYYTTYTN

70 90 110  
ACNAARWSNGAYGGNAARWSNGTNAARAARMGNWSNGTNWSNGARATHCARYTNATGCAY

130 150 170  
AAYYTNGGNAARCAYYTNAAYWSNATGGARMGNGTNGARTGGYTNGMNAARAARYTNCAR

190 210 230  
GAYGTNCAYAAYYTTYGTNGCNYTNGGNGCNCNYTNGCNCNCMNGAYGCNGGNWSNCAR

250 270 290  
MGNCCNMGNAARAARGARGAYAAYGTNYTNGTNGARWSNCAYGARAARWSNYTNGGNGAR

310 330  
GCNGAYAARGCNGAYGTNAAYGTNYTNACNAARGCNAARWSNCARTRR

M = A or C  
R = A or G  
W = A or T  
S = C or G  
Y = C or T  
H = A or C or T  
N = A or G or C or T.

## FIG. 2

DNA sequence for human  
preproparathyroid hormone in plasmid pSSHPTH-10.

10 30 50  
ATGATGATACCTGCAAAAGACATGGCTAAAGTTATGATTGTCATGTTGGCAATTTGTTTT

70 90 110  
CTTACAAAATCGGATGGGAAATCTGTTAAGAAGAGATCTGTGAGTAAAATACAGCTTATG

130 150 170  
CATAACCTGGGAAAACATCTGAACTCGATGGAGAGAGTAGAATGGCTGCGTAAGAAGCTG

190 210 230  
CAGGATGTGCACAATTTTGTGGCCCTTGGAGCTCCTCTAGCTCCCAGAGATGCTGGTTCC

250 270 290  
CAGAGGCCCCGAAAAAAGGAAGACAATGTCTTGGTTGAGAGCCATGAAAAAAGTCTTGGA

310 330  
GAGGCAGACAAAGCTGATGTGAATGTATTAATAAGCTAAATCCCAGTGA

# FIG. 3

Portion of DNA sequence of the plasmid  
for insertion into E. coli, coding for human  
preproparathyroid hormone with flanking sequences.

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      10              30              50
TATGATGATHCCNGCNAARGAYATGGCNAARGTNATGATHGTNATGYTNGCNATHGTGTT

      70              90              110
YYTNACNAARWSNGAYGGNAARWSNGTNAARAARMGNWSNGTNWSNGARATHCARYTNAT

      130             150             170
GCAYAAYYTNGGNAARCAYYTNAAYWSNATGGARMGNGTNGARTGGYTNGNAARAARYT

      190             210             230
NCARGAYGTNCAYAAYYTTYGTNGCNYTNGGNGCNCNYTNGCNCNMGNAYGCNGGNWS

      250             270             290
NCARMGNCCNMGNAARAARGARGAYAAYGTYTNGTNGARWSNCAYGARAARWSNYTNGG

      310             330             350
NGARGCNGAYAARGCNGAYGTNAAYGTNYTNACNAARGCNAARWSNCARTRRAAATGAAA

      370             390             410
ACAGATATTGTCAGAGTTCTGCTCTAGACAGTGTAGGGCAACAATACATGCTGCTAATTC

      430
AAAGCTCTATTA

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M = A or C  
R = A or G  
W = A or T  
S = C or T  
Y = C or T  
H = A or C or T  
N = A or G or C or T.

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**FIG. 4**

DNA sequence for human preproparathyroid hormone in plasmid pSSHPTH-10 with flanking sequences.

10 30 50  
TATGATGATACCTGCAAAAGACATGGCTAAAGTTATGATTGTCATGTTGGCAATTTGTTT

70 90 110  
TCTTACAAAATCGGATGGGAAATCTGTTAAGAAGAGATCTGTGAGTGAAATACAGCTTAT

130 150 170  
GCATAACCTGGGAAAACATCTGAACTCGATGGAGAGAGTAGAATGGCTGCGTAAGAAGCT

190 210 230  
GCAGGATGTGCACAATTTTGTGCCCCTGGAGCTCCTCTAGCTCCCAGAGATGCTGGTTC

250 270 290  
CCAGAGGCCCCGAAAAAAGGAAGACAATGTCTTGGTTGAGAGCCATGAAAAAAGTCTTGG

310 330 350  
AGAGGCAGACAAAGCTGATGTGAATGTATTAATAAGCTAAATCCCAGTGAAAAATGAAA

370 390 410  
ACAGATATTGTCAGAGTTCTGCTCTAGACAGTGTAGGGCAACAATACATGCTGCTAATTC

430  
AAAGCTCTATTA.

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**FIG. 5**

DNA sequence coding for  
preproparathyroid hormone in pSSHPTH-10 with flanking  
sequences, showing the corresponding amino acid  
sequence of preproparathyroid hormone.

10 30 50  
TATGATGATACCTGCAAAAGACATGGCTAAAGTTATGATTGTCATGTTGGCAATTTGTTT  
MetIleProAlaLysAspMetAlaLysValMetIleValMetLeuAlaIleCysPh

70 90 110  
TCTTACAAAATCGGATGGGAAATCTGTTAAGAAGAGATCTGTGAGTGAAATACAGCTTAT  
eLeuThrLysSerAspGlyLysSerValLysLysArgSerValSerGluIleGlnLeuMe

130 150 170  
GCATAACCTGGGAAAACATCTGAACTCGATGGAGAGAGTAGAATGGCTGCGTAAGAAGCT  
tHisAsnLeuGlyLysHisLeuAsnSerMetGluArgValGluTrpLeuArgLysLysLe

190 210 230  
GCAGGATGTGCACAATTTTGTGCCCCTTGGAGCTCCTCTAGCTCCCAGAGATGCTGGTTC  
uGlnAspValHisAsnPheValAlaLeuGlyAlaProLeuAlaProArgAspAlaGlySe

250 270 290  
CCAGAGGCCCGAAAAAAGGAAGACAATGTCTTGTTGAGAGCCATGAAAAAGTCTTGG  
rGlnArgProArgLysLysGluAspAsnValLeuValGluSerHisGluLysSerLeuGl

310 330 350  
AGAGGCAGACAAAGCTGATGTGAATGTATTAATAAGCTAAATCCCAGTGAAAATGAAA  
yGluAlaAspLysAlaAspValAsnValLeuThrLysAlaLysSerGlnEnd

370 390 410  
ACAGATATTGTCAGAGTTCTGCTCTAGACAGTGTAGGGCAACAATACATGCTGCTAATTC

430  
AAAGCTCTATTA.

Figure 6. Nucleotide sequence of the MF 1-HPTH fusion gene from pS LX5-HPTH1. Nucleotide nos. 1-173 make up the MF 1 promoter region and 5' noncoding sequence. 174-440 is the MF 1 N-terminal coding sequence. 441-695 is the HPTH sequence obtained from pSSHPTH-10. 696-726 is an HPTH 3' noncoding sequence from pSSHPTH-10. 727-732 is from pUC19. 733-874 is MF 1 3' noncoding sequence and transcriptional termination signal.

```

10      10      30      50
AGTGCAAGAAAACCAAAAAGCAACAACAGGTTTTGGATAAGTACATATATAAGAGGGCCT

      70      90      110
TTTGTTCCTCATCAAAAATGTTACTGTTCTTACGATTCATTTACGATTCAAGAATAGTTCA

15      130      150      170
AACAAGAAGATTACAACTATCAATTCATACACAATATAAACGACCAAAAAGAATGAGAT

      190      210      230
TTCCTTCAATTTTTACTGCAGTTTTATTTCGCAGCATCCTCCGCATTAGCTGCTCCAGTCA

      250      270      290
ACACTACAACAGAAGATGAAACGGCACAAATTCCGGCTGAAGCTGTCATCGGTTACTCAG

20      310      330      350
ATTTAGAAGGGGATTTTCGATGTTGCTGTTTTGCCATTTTCCAACAGCACAAATAACGGGT

      370      390      410
TATTGTTTATAAATACTACTATTGCCAGCATTGCTGCTAAAGAAGAAGGGGTATCTTTGG

      430      450      470
ATAAAAGAGAGGCTGAAGCTTCTGTGAGTGAAATACAGCTTATGCATAACCTGGGAAAAC

25      490      510      530
ATCTGAACTCGATGGAGAGAGTAGAATGGCTGCGTAAGAAGCTGCAGGATGTGCACAATT

      550      570      590
TTGTTGCCCTTGGAGCTCCTCTAGCTCCCAGAGATGCTGGTTCCCAGAGGCCCCGAAAAA

      610      630      650
AGGAAGACAATGTCTTGGTTGAGAGCCATGAAAAAAGTCTTGGAGAGGCAGACAAAGCTG

      670      690      710
ATGTGAATGTATTAATAAGCTAAATCCAGTGAAAATGAAAACAGATATTGTCAGAGT
5

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730 750 770  
TC1 TTAGAGTCGACTTTGTTCCCACTG TTAGCTCGTACAAAATACAATATAC  
90 810 830  
TTTTCAATTTCTCCGTAAACAACCTGTTTTCCCATGTAATATCCTTTTCTATTTTTCGTTT  
850 870  
CGTTACCAACTTTACACATACTTTATATAGCTAT

10

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Figur 7. Partial DNA s-quence for the plasmid for  
 in- on into yeast in which: cleotide nos. 1-173  
 makes the MF 1 promoter r gion and 5' noncoding  
 sequence. 174-440 is th MF 1 N-terminal coding  
 sequence. 441-695 is an HPTH sequence. 696-726 is an  
 HPTH 3' noncoding sequ nce from pSSHPTH-10. 727-732 is  
 from pUC19. 733-874 is MF 1 3' noncoding sequence and  
 transcriptional termination signal.

10 10 30  
 50  
 AGTGCAAGAAAACCAAAAAGCAACAACAGGTTTTGGATAAGTACATATATAAGAGGGCCT  
 70 90 110  
 TTTGTTCCCATCAAAAATGTTACTGTTCTTACGATTCAATTTACGATTCAAGAATAGTTCA  
 15 130 150 170  
 AACAAGAAGATTACAACTATCAATTTACATACACAATATAAACGACCAAAGAATGAGAT  
 190 210 230  
 TTCCTTCAATTTTTACTGTCAGTTTTATTTCGCAGCATCCTCCGCATTAGCTGCTCCAGTCA  
 250 270 290  
 ACACTACAACAGAAGATGAAACGGCACAAATTCCGGCTGAAGCTGTCATCGGTTA<sup>†</sup>TCAG  
 20 310 330 350  
 ATTTAGAAGGGGATTTTCGATGTTGCTGTTTTGCCATTTTCCAACAGCACAAATAACGGGT  
 370 390 410  
 TATTGTTTATAAATACTACTATTGCCAGCATTGCTGCTAAAGAAGAAGGGGTATCTTTGG  
 430 450 470  
 25 ATAAAAGAGAGGCTGAAGCTWSNGTNWSNGARATHCARYTNATGCAYAAYYTNGGNAARC  
 490 510 530  
 AYYTNAAYWSNATGGARMGNGTNGARTGGYTNMGNAARAARYTNCARGAYGTNCAYAAYT  
 550 570 590  
 TYGTNGCNYTNGGNGCNCNYTNGCNCNMGNAYGCNNGNWSNCARMGNCNMGNAARA  
 610 630 650  
 ARGARGAYAAAYGTNYTNGTNGARWSNCAYGARAARWSNYTNGGNGARGCNGAYAARGCNG  
 670 690 710  
 5 AYGTTAAAYGTNYTNACNAARGCNAARWSNCARTRRAAATGAAAACAGATATTGTCAGAGT

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730 750 770  
TCTC GAGTCGACTTTGTTCCCACTGT TAGCTCGTACAAAATACAATATAC  
90 810 830  
TTTTCAATTTCTCCGTAAACAACCTGTTTTCCCATGTAATATCCTTTTCTATTTTTCGTTT

10

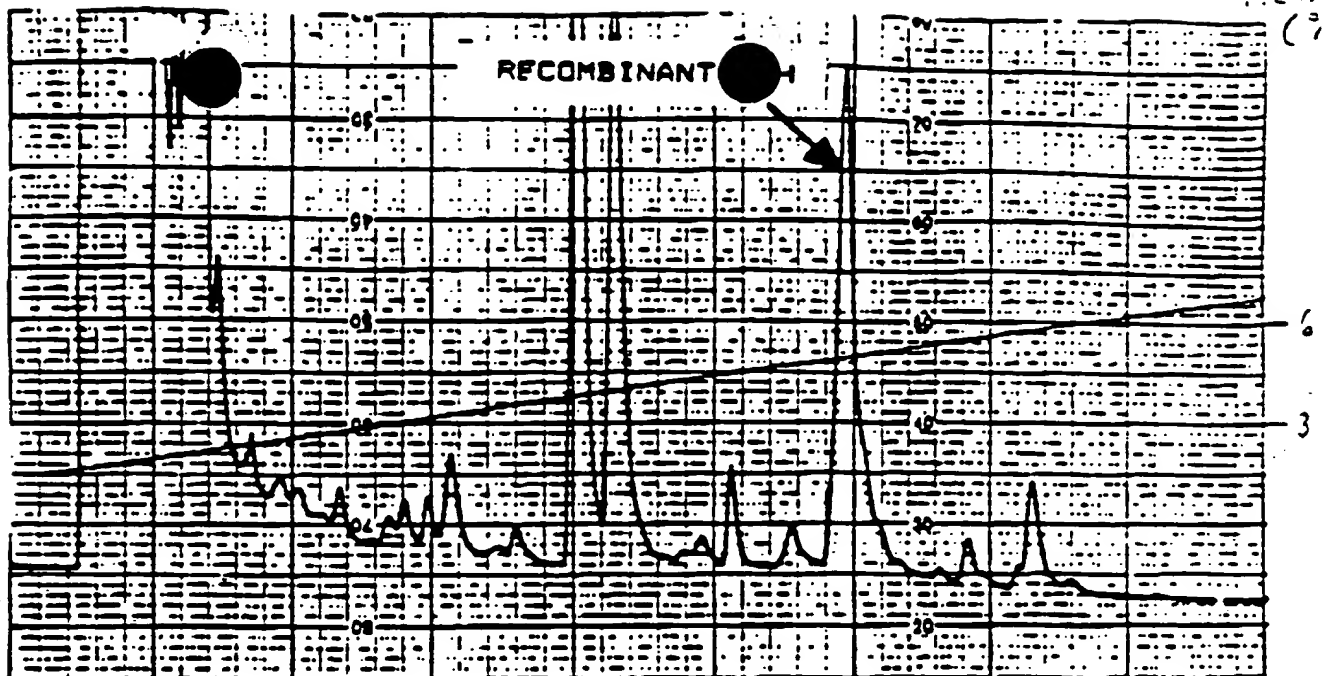
850 870  
CGTTACCAACTTTACACATACTTTATATAGCTAT, wherein

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M = A or C  
R = A or G  
W = A or T  
S = C or G  
Y = C or T  
H = A or C or T  
N = A or G or C or T

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B.

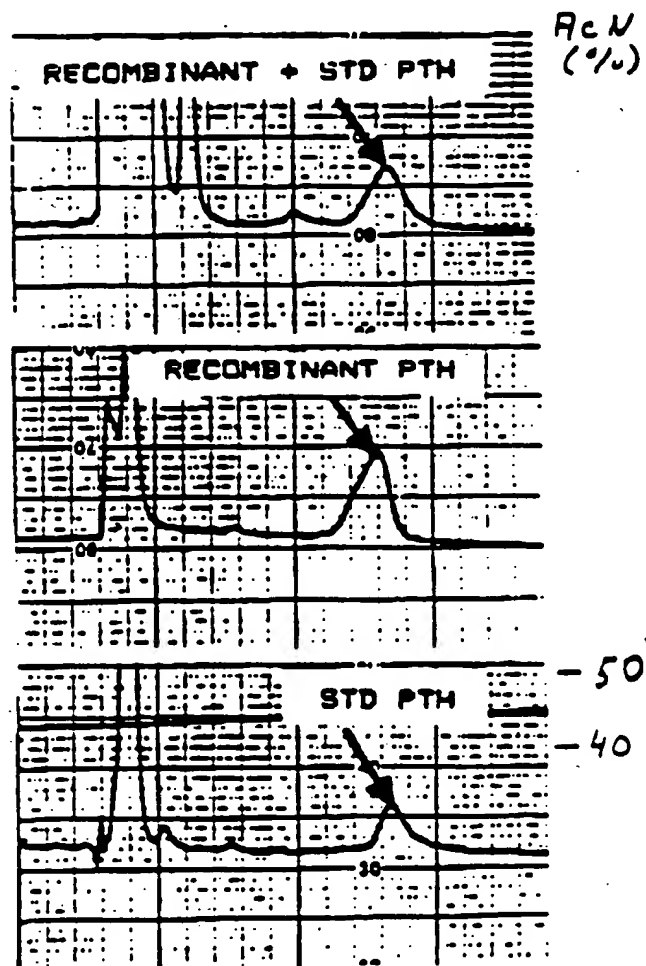


FIG. 9

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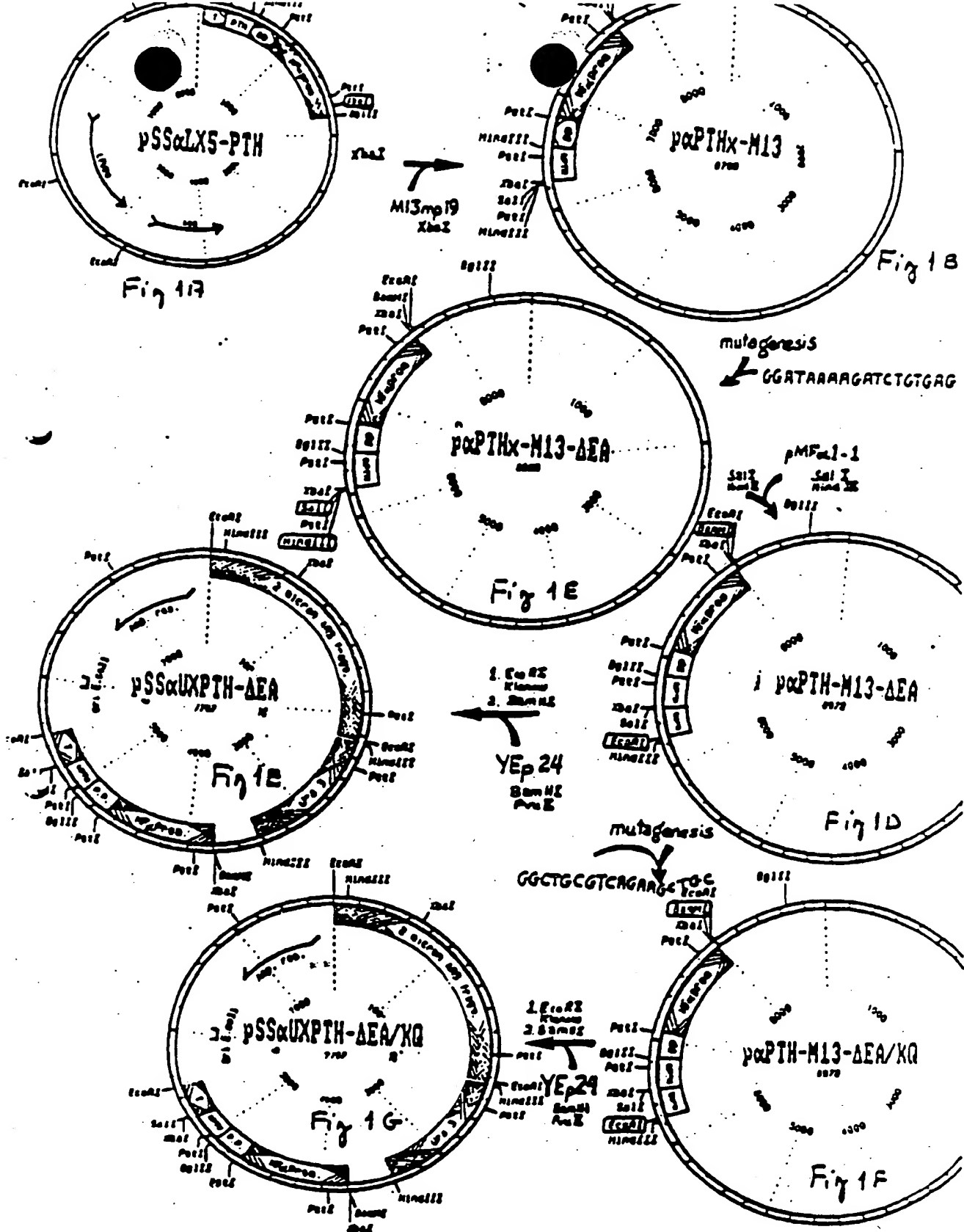
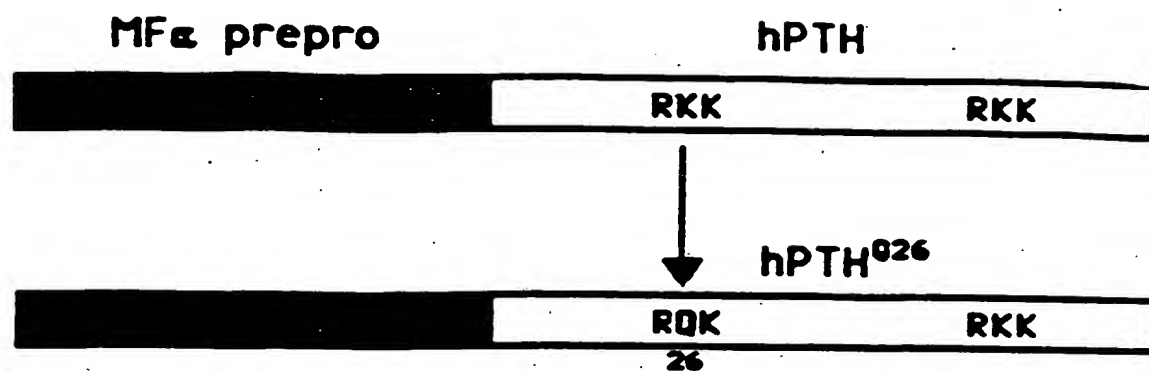


FIG. 10

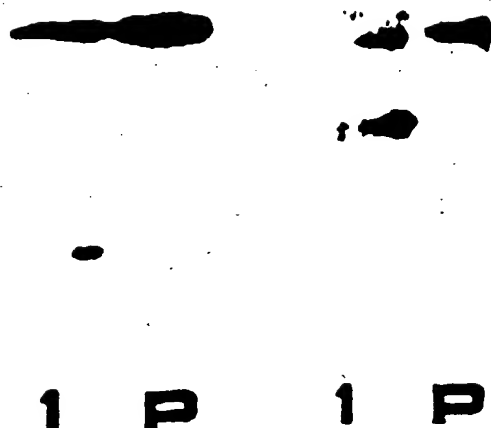
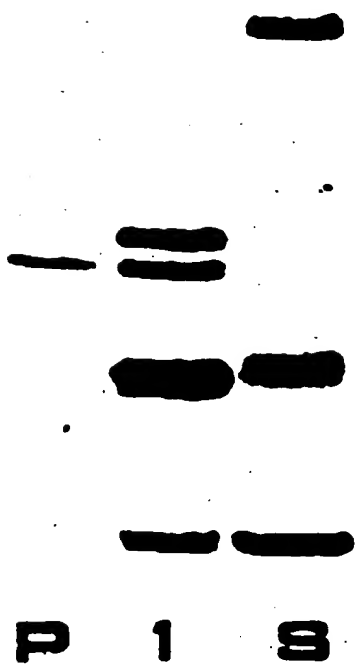


**FIG. 11**

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**a** \_\_\_\_\_

**b** \_\_\_\_\_ **c** \_\_\_\_\_



**FIG. 8**

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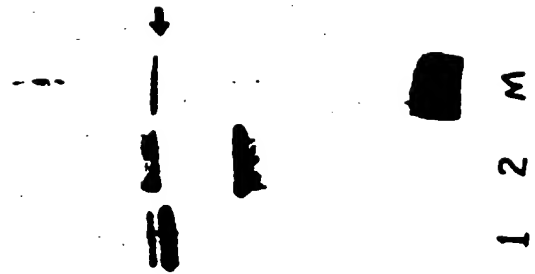
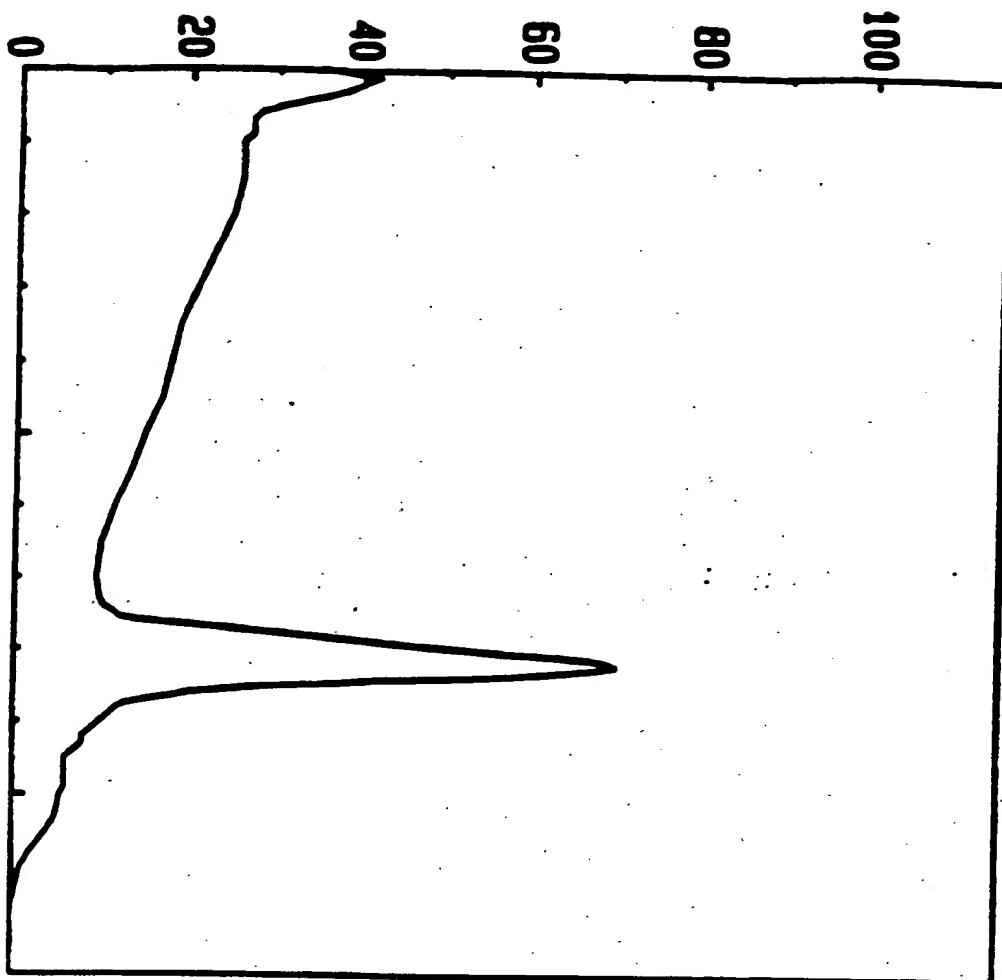


FIG. 12

A

# HPLC CHROMATOGRAM OF hPTH(026)



B



FIG. 13

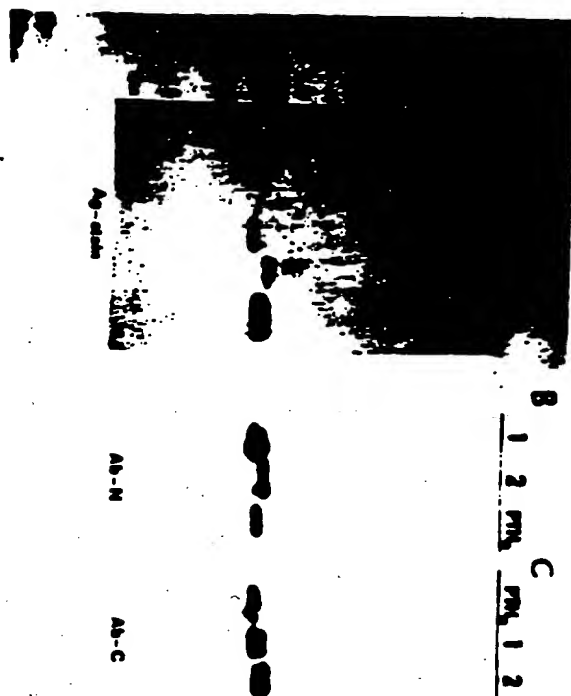
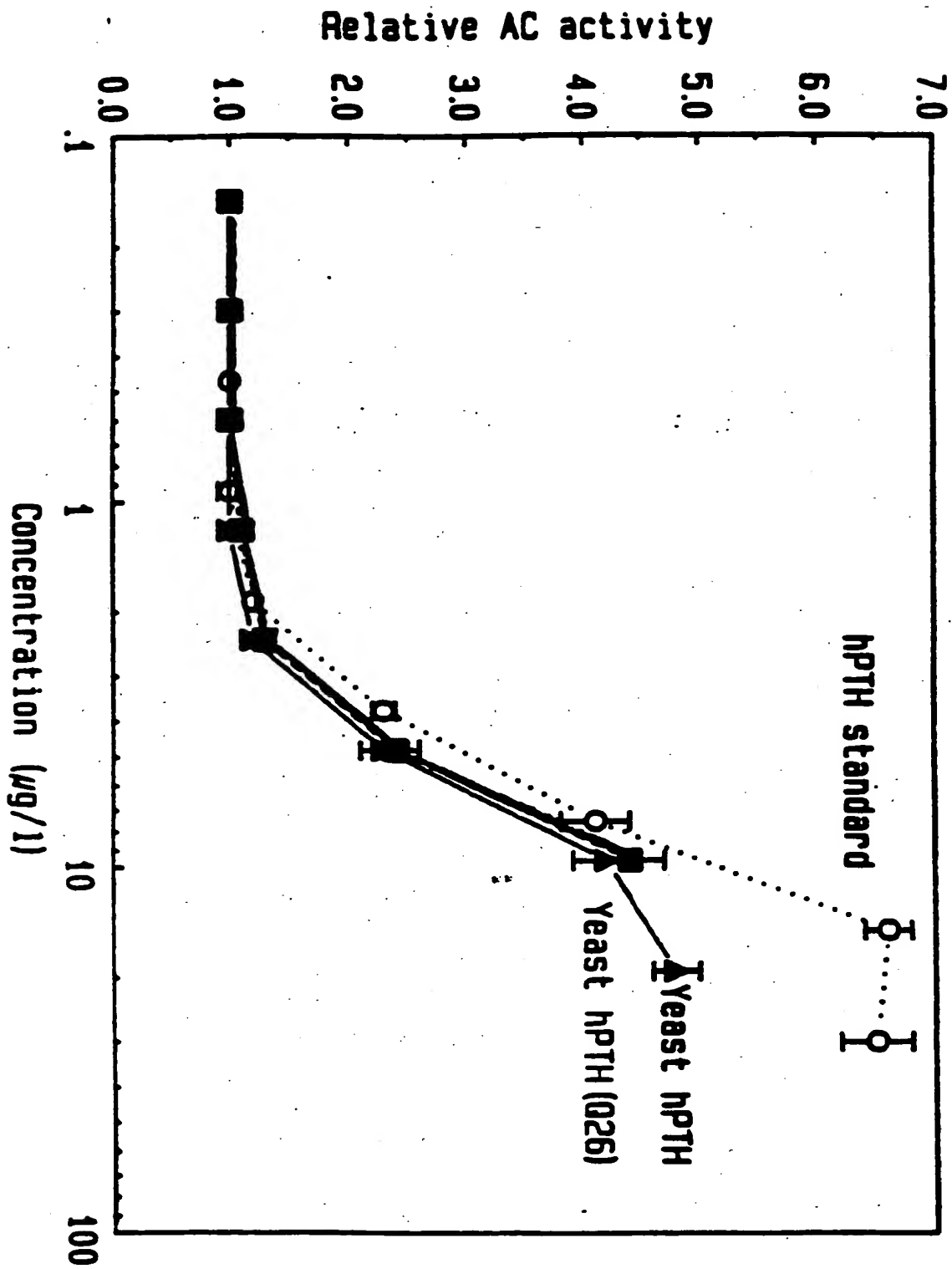


FIG. 14



FIG. 15



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